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iOnctura reaches new clinical milestones in uveal melanoma

- Completed Phase I DIONE-01 study demonstrates clinical activity and long-term safety of roginolisib, a unique allosteric modulator of PI3Kδ
- Patients with uveal melanoma showed a doubling of overall survival compared to historical controls
- Site activation ongoing for randomized Phase II OCULE-01 study in uveal melanoma

Geneva, Switzerland and Amsterdam, The Netherlands, 11 Dec 2024 - iOnctura, a clinical-stage biopharmaceutical company combating neglected and hard-to-treat cancers, today provides a clinical update on its lead asset, roginolisib. Results from the completed Phase I DIONE-01 study are due to be presented at the European Society for Medical Oncology Immuno-Oncology (ESMO-IO) annual congress tomorrow, 12 December at 12:30 CET (presentation 164P).

Allosteric modulator of PI3Kδ, roginolisib, has a unique chemical structure and binding mechanism which makes it highly specific for PI3Kδ, giving it an advantageous pharmacology profile and an unprecedented safety profile compared to previous generations of PI3Kδ inhibitors.

Roginolisib is being investigated in solid and hematological malignancies including uveal melanoma (UM), a rare cancer of the eye. Eye melanoma is a rapidly growing market which is projected to be worth USD 9.56B by 2032[1].

The two-part Phase I study DIONE-01, firstly evaluated continuous daily dosing of roginolisib [at 10, 20, 40 and 80 mg] in 24 patients with pretreated solid tumors and follicular lymphoma (FL), and secondly evaluated a dose confirmation cohort in 20 UM patients.

Results from DIONE-01 show:

- Study met its primary objective to determine the safety of the anticipated optimal biologically effective dose (BED): Roginolisib was well tolerated at the recommended Phase II dose (RP2D) of 80mg, with <7% Grade 3/4 treatment-emergent adverse events (TEAEs) considered to be related to roginolisib. TEAEs did not result in immune-related toxicity, or dose-limiting toxicity, in either solid tumor or hematological patients. In contrast to prior PI3Kδ inhibitors, roginolisib dosing did not require dose modifications.
- Roginolisib is well tolerated over long periods of treatment, up to 4.5 years.

[1] Emergen Research, Jan 2024

- Median overall survival (OS) was 16 months for the 29 patients with UM treated with roginolisib, who had previously received a median of two prior therapies. This exceeds the median OS of 7 months observed in historical controls in patients receiving immunotherapies as second line treatment[2].
- Median progression free survival (PFS) was 5 months for patients treated with roginolisib versus less than 3 months for historical controls[2].
- Clinical findings validate the mechanism of action of roginolisib: roginolisib reduces immune-suppressive immune cells and chemokines, UM-related tumor clones (ctDNA) and PI3K-related signaling indicating a rebalancing of the immune system.

Catherine Pickering, Chief Executive Officer of iOnctura, said: "The Phase I DIONE-01 data highlight the benefits of roginolisib for patients with uveal melanoma and advanced cancers. Roginolisib's unique allosteric binding mechanism has translated into a differentiated beneficial clinical profile, including a doubling of overall survival compared to historical controls in uveal melanoma. We are delighted to announce these data support progression of roginolisib into a randomized Phase II study."

Professor Michele Maio, University of Siena and Principal Investigator of the roginolisib studies, added: "Being able to continue to investigate roginolisib in a randomized Phase II study is a positive step to understand more about this already well tolerated molecule. Roginolisib has given prolonged disease stabilization to patients with uveal melanoma who have exhausted all other therapeutic options. So far, these patients have maintained a good quality of life without major limitations. I'm looking forward to seeing what the Phase II trial delivers over the coming months."

Activation of trial sites for the Phase II OCULE-01 study (NCT06717126) investigating roginolisib versus investigator's choice in the second-line+ treatment of uveal melanoma is ongoing.

ENDS

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[2] Rantala et al., Melanoma Res., 2019 Dec 29(6):561-568

About iOnctura

iOnctura is a clinical-stage biopharmaceutical company combating neglected and hard-to-treat cancers with precision oral small molecules that target cancers in novel ways. The bold new treatments extend lives and improve healthspans, changing the outlook for patients and their families. Two therapeutic candidates have progressed into mid-stage clinical development: roginolisib is the first allosteric modulator of PI3Kδ; and cambritaxestat is the only autotaxin inhibitor in clinical development to treat cancer. iOnctura BV is headquartered in Amsterdam, The Netherlands with its wholly owned Swiss subsidiary, iOnctura SA, located in Geneva, Switzerland. iOnctura is backed by specialist institutional investors including Syncona, EIC Fund, M Ventures, Inkef Capital, VI Partners and Schroders Capital.

About roginolisib

Roginolisib is an allosteric modulator of PI3Kδ with a unique chemical structure and binding mode. The PI3K signaling pathway is one of the most commonly dysregulated pathways in cancer and the precise targeting of the PI3Kδ isoform delivers substantial anti-tumor effects with a low-toxicity profile. Clinical data have demonstrated roginolisib's excellent safety profile and sustained clinical activity in uveal melanoma (UM), a rare eye cancer with few available treatments. Site activation for the randomized Phase II OCULE-01 study in uveal melanoma is ongoing, and Phase II studies in other cancers, including non-small cell lung cancer and myelofibrosis, are in planning.

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